1: Hepatology 1995 Feb;21(2):561-9

Pathogenesis of diquat-induced liver necrosis in selenium-deficient rats: assessment of the roles of lipid peroxidation and selenoprotein P.

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A dose of diquat below the amount injurious to selenium-replete animals causes lipid peroxidation and massive liver necrosis in selenium-deficient rats. The current study was undertaken to characterize the lipid peroxidation with respect to the liver injury and to correlate the presence of several selenoproteins with the protective effect of selenium. Lipid peroxidation was assessed by measurement of F2 isoprostanes. Diquat caused an increase in liver and plasma F2 isoprotanes. A gradient of these compounds was detected across the liver in some animals, indicating that this organ was a source of some of the plasma F2 isoprostanes. A time-course experiment showed that liver F2 isoprostane concentration increased before plasma alanine transaminase (ALT) levels rose. Selenium-deficient rats were injected with selenium doses from 2 to 50 micrograms/kg and studied 12 hours later. A dose of 10 micrograms/kg or more prevented diquat-induced lipid peroxidation and liver injury. This dose increased plasma selenoprotein P substantially, and a dose-response was present. Liver cellular and plasma glutathione peroxidase activities remained below 2% of their values in control rats for all selenium doses. In selenium-deficient rats given diquat, hepatic lipid peroxidation precedes hepatic necrosis and could therefore be an important mechanism of the necrosis. Selenoprotein P levels were increased by selenium injections, which protected against diquat injury, but glutathione peroxidase activity was not increased. This is consistent with selenoprotein P being the mediator of the selenium effect.

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☐ 1: Cell Mol Life Sci 2000 Dec;57(13-14):1836-45 Related Articles, Books, LinkOut

Selenoprotein P.

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Selenoprotein P (SeP) is an extracellular, monomeric glycoprotein containing up to 10 selenocysteine residues in the polypeptide chain. It is ubiquitously expressed in mammalian tissues, and in human plasma it accounts for at least 40% of the total selenium concentration. SeP binds to heparin and cell membranes, and is associated with endothelial cells. SeP in human plasma protects against peroxynitrite-mediated oxidation and reduces phospholipid hydroperoxide in vitro, in accordance with the presumption that it has a function as an extracellular oxidant defense. Immunochemical assays have demonstrated that its concentration in plasma varies much with selenium intake, but other factors also have an influence.

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